



Best K, Rankin J. [Long-term survival for individuals born with congenital heart disease: A systematic review and meta-analysis](#). *Journal of the American Heart Association* 2016, 5(6), e002846.

Copyright:

© 2016 The Authors. Published on behalf of the American Heart Association, Inc., by Wiley Blackwell. This is an open access article under the terms of the [Creative Commons Attribution-NonCommercial](#) License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

DOI link to article:

<http://dx.doi.org/10.1161/JAHA.115.002846>

Date deposited:

27/07/2016



This work is licensed under a [Creative Commons Attribution-NonCommercial 3.0 Unported License](#)

Long-Term Survival of Individuals Born With Congenital Heart Disease: A Systematic Review and Meta-Analysis

Katie E. Best, PhD; Judith Rankin, PhD

Background—Estimates of long-term survival are required to adequately assess the variety of health and social services required by those with congenital heart disease (CHD) throughout their lives.

Methods and Results—Medline, Embase, and Scopus were searched from inception to June 2015 using MeSH headings and keywords. Population-based studies that ascertained all persons born with CHD within a predefined area and reported survival estimates at ≥ 5 years were included. Unadjusted survival estimates for each CHD subtype at ages 1 year, 5 years, 10 years, and so forth were extracted. Pooled survival estimates for each age were calculated using meta-analyses. Metaregression was performed to examine the impact of study period on survival. Of 7840 identified articles, 16 met the inclusion criteria. Among those with CHD, pooled 1-year survival was 87.0% (95% CI 82.1–91.2), pooled 5-year survival was 85.4% (95% CI 79.4–90.5), and pooled 10-year survival was 81.4% (95% CI 73.8–87.9). There was significant heterogeneity of survival estimates among articles ($P < 0.001$ for 1-, 5-, and 10-year survival). A more recent study period was significantly associated with greater survival at ages 1 year ($P = 0.047$), 5 years ($P = 0.013$), and 10 years ($P = 0.046$). Survival varied by CHD subtype, with 5-year survival being greatest for those with ventricular septal defect (96.3%, 95% CI 93.7–98.2) and lowest for those with hypoplastic left heart (12.5%, 95% CI 0.0–41.4).

Conclusions—Among persons with CHD, the mortality rate is greatest during the first year of life; however, this systematic review and meta-analysis showed that survival decreases gradually after infancy and into adulthood. (*J Am Heart Assoc.* 2016;5:e002846 doi: 10.1161/JAHA.115.002846)

Key Words: congenital • heart defects • survival

Congenital heart disease (CHD) composes the largest group of congenital anomalies and affects $\approx 1\%$ of births in the United States and Europe.^{1–3} CHD is a leading cause of stillbirth and infant death and accounts for 4.2% of neonatal deaths in the United States.⁴ Babies with severe CHD subtypes require complex surgeries for survival. With advances in medical, surgical, and intensive care interventions, an estimated 83% of babies with CHD now survive infancy in the United States.⁵ Although 1-year survival estimates have been described,^{3,6–11} long-term survival estimates are not well researched, and survival may continue to decrease into adulthood.

A previous systematic review of the long-term prognosis of CHD included only hospital-based studies that

ascertained cases postsurgically or in adulthood; estimates were not representative of all persons with CHD.¹² We conducted a systematic review and meta-analysis of population-based studies reporting long-term survival of persons born with CHD. The aim was to assess and quantify long-term survival to inform health services planning and decision making.

Methods

Search Strategy

We conducted comprehensive literature searches of Medline, Embase, and Scopus from inception (1946, 1974, and 1996, respectively) to June 18, 2015. MeSH terms and keywords were entered systematically into the databases. The keywords included *congenital* and *heart* or *cardiac* or *cardiovascular* and subject heading searches such as “exp Heart Defects, Congenital/ep, mo” but varied according to database. The list of search terms is available from the authors.

After systematic searches of each database, the citations were extracted, and titles and abstracts were screened according to the inclusion criteria. Full articles were retrieved for all relevant citations. Reference lists of included articles

From the Institute of Health & Society, Newcastle University, Newcastle upon Tyne, UK.

Correspondence to: Kate Elizabeth Best, PhD, Institute of Health & Society, Baddiley-Clark Building, Newcastle University, Newcastle upon Tyne NE2 4AX, UK. E-mail: kate.best@ncl.ac.uk

Received November 5, 2015; accepted February 19, 2016.

© 2016 The Authors. Published on behalf of the American Heart Association, Inc., by Wiley Blackwell. This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

were scanned and examined, and key journals were searched using keywords.

Inclusion Criteria

Population-based original studies were included if they (1) ascertained all persons born with CHD within a predefined geopolitical area; (2) reported survival estimates (or the number of patients born and the number or proportion alive) at age ≥ 5 years; (3) reported survival estimates for all CHD combined or a single CHD subtype including ventricular septal defect, pulmonary valve stenosis, atrial septal defect, aortic valve atresia or stenosis, atrioventricular septal defect, coarctation of aorta, common arterial truncus, pulmonary valve atresia (with ventricular septal defect or with intact ventricular septum), tetralogy of Fallot, total anomalous pulmonary venous return, transposition of great vessels, tricuspid atresia, single ventricle, hypoplastic left heart, and Ebstein's anomaly; (4) were available from the British Library or the Internet and were written in the English language.

Exclusion Criteria

Articles were excluded if patients were not followed from birth (eg, follow-up began in adulthood or after surgical correction); patients were not born in well-defined regions (ie, hospital-based); survival was not estimated as a proportion of those born with CHD (eg, age-specific population mortality rates); survival was reported only for certain subtype groups (eg, "severe" CHD). For multiple articles reported on the same data set, the largest study or the study with the most recent study period was included. Both articles were included if they reported survival for different CHD subtypes or ages.

Data Extraction

K.E.B. performed the literature searches, screened citations, and reviewed 40 full papers. J.R. screened 10% of the titles and all abstracts to confirm decisions about inclusion, and extracted data from all included papers. There were no discrepancies between reviewers regarding article inclusion.

Study characteristics including study design, quality, data sources, prevalence estimates, and the percentage of cases with extracardiac anomalies (ie, cases of CHD occurring with another congenital anomaly not of the cardiovascular system, such as Down syndrome or cleft lip) were extracted from each article. If it was unclear whether cases with extracardiac anomalies were included, the authors were contacted.

Kaplan–Meier survival estimates and corresponding 95% CIs were obtained from each included study at ages 1 year, 5 years, 10 years, and so forth. If 95% CIs were not reported, the authors were contacted. If this was unsuccessful, the number of

patients born and the proportion that survived were used to estimate binomial 95% CIs, assuming no cases were censored. Survival estimates for all CHD subtypes combined and for each CHD subtype were extracted. If survival estimates were presented only graphically, the authors were contacted for survival estimates. If this was unsuccessful, survival estimates were extracted using Plot Digitizer software.^{13,14}

Statistical Analysis

If there were at least 3 studies reporting survival, pooled estimates of survival were calculated using a meta-analysis with random effects. Weighting for each article was allocated using the inverse of the variance. If the number of studies is small, the estimation of between-study variance is thought to be imprecise in random-effects models.¹⁵ Consequently, if there were only 3 studies reporting survival, the pooled survival was also estimated using fixed-effects meta-analysis to allow comparison. To stabilize the variance and adjust the study weights, a simplified double-arcsine transformation was performed on the survival estimates and 95% CIs.¹⁶ The Cochrane Q test and the I^2 statistic were used to test for heterogeneity in survival estimates between articles, with $I^2 > 50\%$ indicating substantial heterogeneity.¹⁷ Random-effects metaregression was performed for all CHD subtypes combined to assess year of delivery as a source of heterogeneity. In this analysis, the year in which the study commenced was used as an explanatory variable. The adjusted R^2 value was used to estimate the proportion of between-article variation accounted for by the year of study commencement. A bubble plot was used to present the fitted metaregression model. In this analysis, bubbles represent each article, with sizes dependent on the

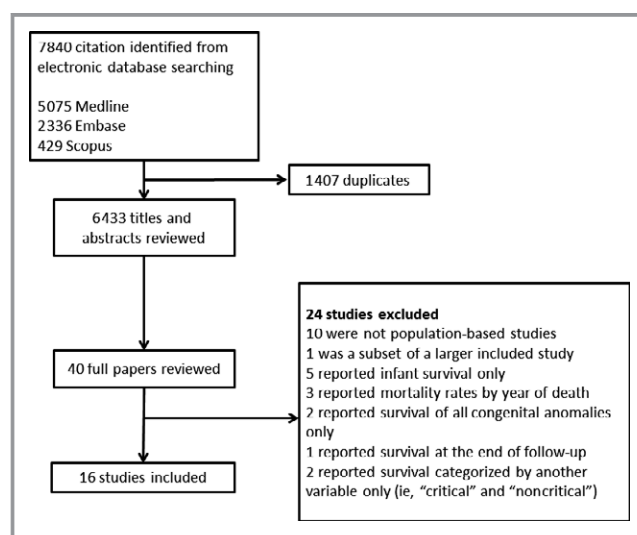


Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses diagram for the flow of articles through the review.

Table 1. Descriptions of the Included Articles

Study	Included Birth Years	Study Location	Included CHD Subtypes (ICD Codes)	Inclusion of ECAs	Age Limit for Diagnosis	Source of Cases	Source of Death Information	Percentage of Traced Cases	Prevalence per 1000 Live Births
Dastgiri et al ²⁰	1980–1997	Glasgow, Scotland	All CHD subtypes (ICD 10: Q20–26)	Author's response: excluded	No age limit	Glasgow register of Congenital Anomalies	Registrar General for Scotland	97% (all congenital anomalies)	Not stated
Fixler et al ²¹	1996–2003	Texas, USA	SV physiology: HLH (ICD 9: 746.7), PVA-IVS (746.0), SV (745.3), TA (746.1), d-TGV (745.1)	Cases with trisomy 13 or 18 were excluded; 14.1% of HLH, 21.0% of SV, 15.3% of PVA-IVS, 17.9% of TA, 9.3% of d-TGV had ECAs	1 year	Texas Birth Defects Registry	Medical records, death certificates, national death index	N/A, nontraced cases considered alive	Not stated
Frid et al ²²	1973–1997	Sweden	AVSD (ICD 9: 745G, ICD 10: 21.2)	Cases with trisomy 13 or 18 were excluded; 68.9% had trisomy 21	None stated	Register of Congenital Malformations, Register of Congenital Heart Malformations, and the Medical Birth Register; local registries at 4 pediatric cardiology centers were also searched for the beginning of the study period	National population database and medical records	98.7% of all cases with AVSD	0.3
Garne ²³	1986–1998	Funen County, Denmark	All CHD subtypes (EUROCAT criteria ie, ICD 10: Q20–26)	Cases with ECAs were included, 21% of cases	5 years and diagnosed before 2002	EUROCAT Registry of Congenital Malformations for Funen County	National registration system	99.6%	7.9
Idom et al ²⁴	1977–2009	Denmark, Europe	HLH (ICD 10: Q234), PVA-IVS (Q220), TA (Q224)	Cases with ECAs were included, 10% of cases	All ages	Danish register of congenital heart disease, local surgical registries, medical records, local fetal ultrasound registries	Civil registration system	Not stated	0.4
Jackson et al ²⁵	1979–1988	Merseyside, England	All CHD subtypes (ICD 9: 745.00–747.49)	Cases with ECAs were included, percentage not stated	No age limit	Liverpool Registry of Congenital Malformations	Liverpool Registry of Congenital Malformations and hospital records	Not stated	7.6
Meberg et al ²⁶	1982–1996	Vestfold, Norway, Europe	All CHD subtypes (no ICD codes stated)	Cases with ECAs were included, 20% of cases	None stated	Vestfold County Central Hospital, regional cardiology services, Child Health Centers and pediatric departments of the hospitals in neighboring counties	Hospital records	100%	10.2

Continued

Table 1. Continued

Study	Included Birth Years	Study Location	Included CHD Subtypes (ICD Codes)	Inclusion of ECAs	Age Limit for Diagnosis	Source of Cases	Source of Death Information	Percentage of Traced Cases	Prevalence per 1000 Live Births
Miller et al ²⁷	1979–2003	Metropolitan Atlanta, GA, USA	AVSD (ICD 9: 745.000–747.999)	Cases with trisomy 13 or 18 were excluded, 52.4% had trisomy 21	None stated	Metropolitan Atlanta Congenital Defects Program	Hospital records and vital records from the state of Georgia, National Death Index	Not stated but number of untraced “assumed to be small”	Not stated
Moons et al ²⁸	2002	Belgium	All CHD subtypes (no ICD codes specified)	Author response: cases with ECAs were included, percentage not stated	5 years	Pediatric cardiology database covering 7 tertiary care centers in Belgium	Medical records	Not stated	8.3
Nembhard et al ²⁹	1996–2003	Texas, USA	ICD 9 (746–747)	Cases with trisomy 13 or 18 were excluded, 20.7% of cases had ECAs	1 year	Texas birth defects register	Death certificates linked to the Texas birth defects register	Not stated	8.7
Olsen et al ³⁰	1977–2006	Denmark	All CHD subtypes: ICD 8: 746 to 747 (except 746.7 and 747.5–747.9) and ICD-10: Q20–Q26 (except Q26.5–Q26.6)	Cases with ECAs were included, 20.0% of cases	1 year	Danish National Registry of Patients	Civil registration system	100%	3.7
Samaneek and Voriskova ³¹	1980–1990	Bohemia, Czech Republic	All CHD subtypes (no ICD codes specified)	Not stated	None stated	Hospital records	Autopsy reports	Not stated	6.2
Ternant et al ³²	1985–2003	Northeast England	All CHD subtypes (ICD 10: Q20–26)	Cases with ECAs were excluded, percentage not stated	16 years of age (1985–2001) or, from 2001, to age 12 years	Northern Congenital Abnormality Survey	Office for National Statistics death registrations	99% (of all congenital anomalies)	6.8
Wang et al (2011) ³³	1983–2006	New York State, USA	TGV (ICD 9: 745.10–745.12, 745.19), ToF (745.2), HLH (746.7), AVA/S (746.3), CAT (745.0), AVSD (745.6), CoA (747.10)	Cases with ECAs were included, percentage not stated	None stated	Congenital Malformations Registry	Death certificates files maintained by the New York State Department of Health	97% (of all congenital anomalies)	9.5

Continued

Table 1. Continued

Study	Included Birth Years	Study Location	Included CHD Subtypes (ICD Codes)	Inclusion of ECAs	Age Limit for Diagnosis	Source of Cases	Source of Death Information	Percentage of Traced Cases	Prevalence per 1000 Live Births
Wang et al (2013) ³⁴	1983–2006	New York State, USA	TGV (ICD 9: 745.10–745.12, 745.19), ToF (745.2), HLH (746.7), CoA (747.10)	Cases with ECAs were included, percentage not stated	2 years	Congenital Malformations Registry	Death certificate files maintained by the New York State Department of Health	Not stated	Not stated
Wang et al (2015) ³⁵	1991–2007	Arizona, Colorado, Florida, Georgia (5 counties of Metropolitan Atlanta), Illinois, Massachusetts, Michigan, Nebraska, New Jersey, New York (excluding New York City), North Carolina, Texas	TGV (ICD 9: 745.10–745.12, 745.19), ToF (745.2), HLH (746.7), AVA/S (746.3), CAT (745.0), AVSD (745.6), CoA (747.10)	Cases with ECAs included, percentage not stated	None stated	Arizona Birth Defects Monitoring Program, Metropolitan Atlanta Congenital Defects Program, Colorado Responds to Children with Special Needs, Florida Birth Defects Registry, Illinois Adverse Pregnancy Outcomes Reporting System, Massachusetts Birth Defects Monitoring Program, Michigan Birth Defects Registry, Nebraska Birth Defects Registry, New Jersey Special Child Health Services Registry, New York State Congenital Malformations Registry, North Carolina Birth Defects Monitoring Program, and Texas Birth Defects Epidemiology and Surveillance Branch	Death certificates, hospital discharge files (Arizona, Texas), medical records (Arizona, Texas), and the National Death Index (Georgia, Michigan)	Not stated	2.1

AVA/S, aortic valve atresia or stenosis; AVSD, atrioventricular septal defect; CAT, common arterial trunk; CHD, congenital heart disease; CoA, coarctation of aorta; d-TGV, dextro-TGV; ECA, extracardiac anomaly; HLH, hypoplastic left heart; ICD, International Classification of Disease; IVS, intact ventricular septum; N/A, not available; PVA, pulmonary valve atresia (with ventricular septal defect or IVS); SV, single ventricle; TA, tricuspid atresia; TGV, transposition of great vessels; ToF, tetralogy of Fallot.

precision of the survival estimates. Publication bias was assessed with the Egger test.¹⁸

Analysis was performed in Stata 13 (StataCorp), and $P < 0.05$ was considered statistically significant.

Quality Appraisal

Quality appraisal was based on 4 of the 6 domains developed by Hayden et al to assess potential bias in systematic reviews of prognostic studies.¹⁹ The domains used were study ascertainment, study attrition, outcome ascertainment, and analysis. The domains relating to confounding and prognostic factors were not relevant to this review because the primary aim was to investigate unadjusted survival estimates.

Results

Figure 1 shows a Preferred Reporting Items for Systematic Reviews and Meta-Analyses diagram for the flow of articles through the review. Of 7840 identified articles, 16 met the inclusion criteria.^{20–35}

Study Characteristics

All included studies were conducted in high-income Western populations, with 10 in Europe and 6 in the United States (Table 1). Although several articles reported survival of subsets of the same population, all were included because survival was reported for different CHD subtypes or at different ages. The oldest article included patients born between 1973 and 1997,²² and the most recent article included patients born between 1991 and 2007.³⁵ Of the 16 included articles, 9 included cases with extracardiac anomalies, with $\approx 20\%$ of cases occurring with other congenital anomalies in each article.^{23–26,28,30,33–35} Four articles excluded patients with trisomy 13 (Patau syndrome) and 18 (Edward syndrome) only.^{21,22,27,29} Two articles excluded cases of CHD with any extracardiac anomalies,^{20,32} and 1 did not state whether cases with extracardiac anomalies were included.³¹ Prevalence estimates were reported by most studies and ranged from 3.7³⁰ to 10.2²⁶ per 1000 live births when considering all CHD as a composite group.

Survival Estimates

Survival was reported to age 5 years in 5 articles,^{20,21,23,28,29} to age 8 years in 1 article,³⁵ to age 10 years in 3 articles,^{25–27} to age 15 years in 2 articles,^{22,31} to age 20 years in 1 article,³² to age 25 years in 3 articles,^{30,33,34} and to age 30 years in 1 article.²⁴

For all CHD (as a composite group), pooled 1-year survival from 6 articles was 87.0% (95% CI 82.1–91.2), pooled 5-year

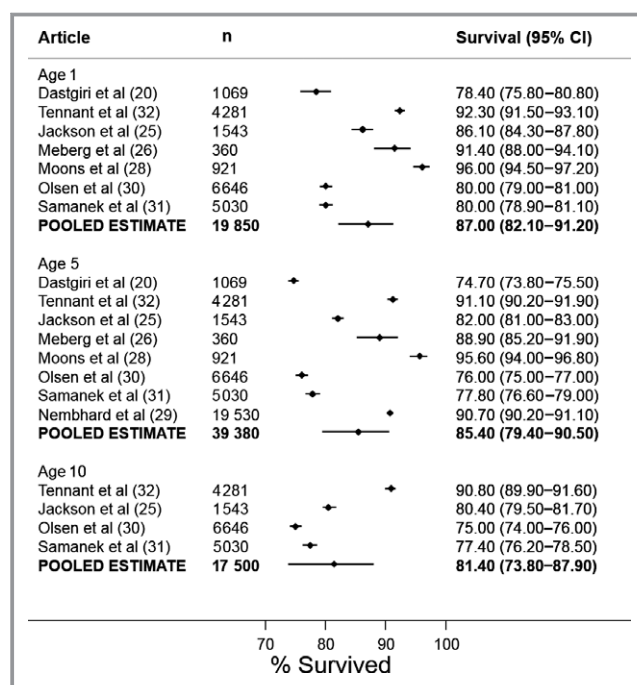


Figure 2. Forest plot for all congenital heart disease at ages 1, 5, and 10 years.

survival from 8 articles was 85.4% (95% CI 79.4–90.5), and pooled 10-year survival from 4 articles was 81.4% (95% CI 73.8–87.9) (Figure 2). It was not possible to pool estimates beyond 10 years because there were too few articles; however, Figure 3 shows the survival estimates plotted over increasing age, up to age 25 years. The fitted metaregression showed that survival decreases very gradually with increasing age over 25 years. There was no evidence of publication bias according to Egger tests ($P=0.748$ for 1 year, $P=0.237$ for 5 years, and $P=0.601$ for 10 years). There was significant

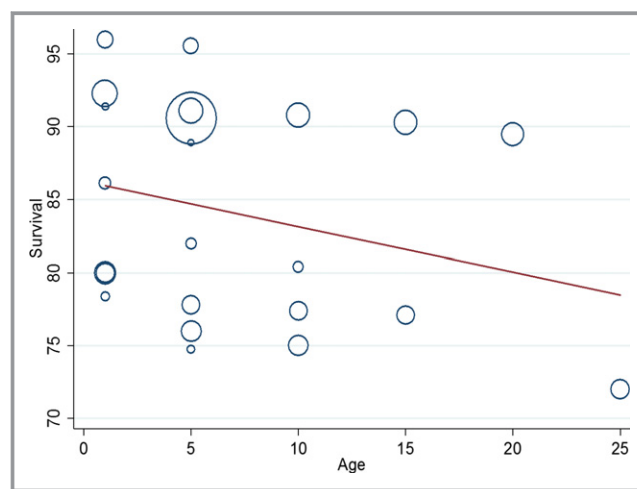


Figure 3. Bubble plot of survival estimates for all congenital heart disease at ages 1 to 25 years.

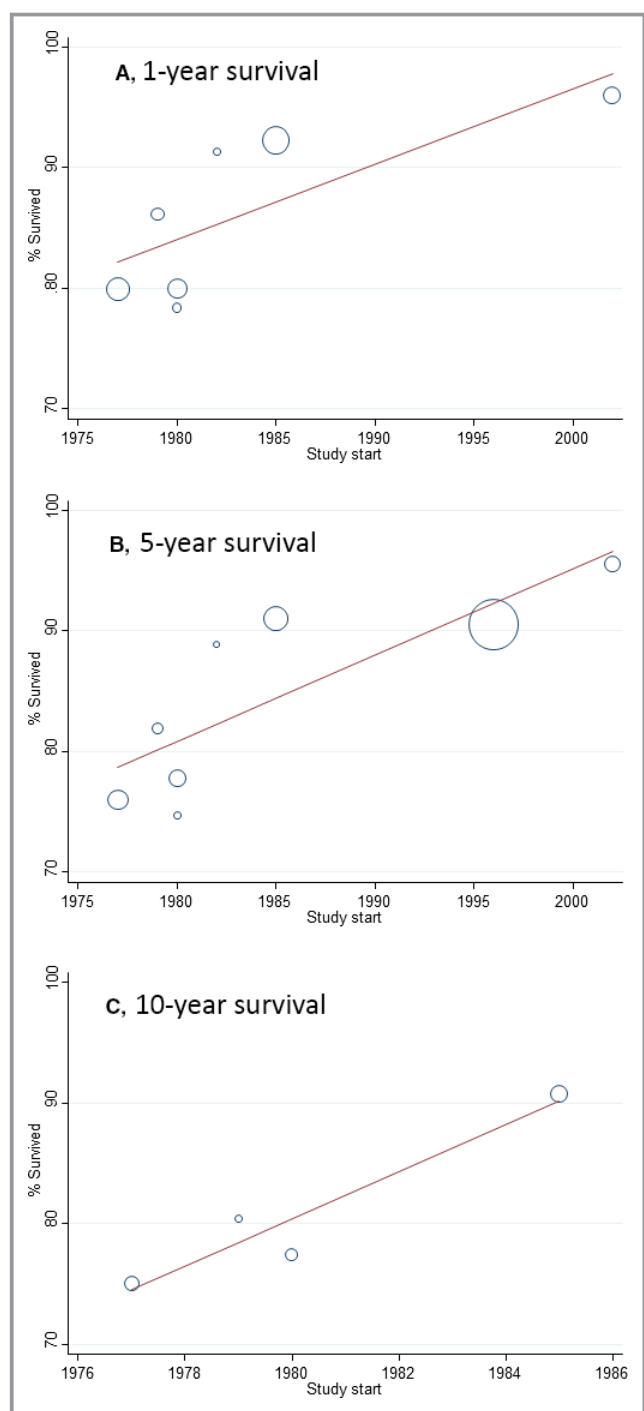


Figure 4. Bubble plots showing the association between study period and survival for all congenital heart disease. A, 1-year survival. B, 5-year survival. C, 10-year survival.

heterogeneity between articles for survival at 1 year ($I^2=99.0\%$, $P<0.001$), 5 years ($I^2=99.6\%$, $P<0.001$), and 10 years ($I^2=99.5\%$, $P<0.001$). Metaregression showed that a more recent study period was significantly associated with increased 1-, 5-, and 10-year survival ($P=0.047$, $P=0.013$, and $P=0.046$, respectively) (Figure 4). According to the adjusted

R^2 values, study period accounted for 50.9%, 62.8%, and 87.0% of the between-article variance for 1-, 5-, and 10-year survival. After adjustment for study period, however, substantial residual heterogeneity remained that was attributable to between-study heterogeneity ($I^2=98.2\%$ at age 1 year, $I^2=98.4\%$ for survival at age 5 years, and $I^2=93.7\%$ for survival at age 10 years).

Table 2 shows the survival estimates and pooled survival estimates for persons with CHD by subtype. Pooled 1-year survival was lowest for those with hypoplastic left heart (17.4%, 95% CI 0.0–54.5) and greatest for those with ventricular septal defect (95.5%, 95% CI 89.0–99.2). There was significant heterogeneity of survival estimates among articles for all CHD subtypes, with the exception of tetralogy of Fallot ($I^2=0\%$, $P=0.169$). Heterogeneity of estimates for single ventricle was of borderline statistical significance ($I^2=65.0\%$, $P=0.057$). Pooled 5-year survival varied by subtype, with survival for hypoplastic left heart at 12.5% (95% CI 0.0–41.4) and survival for ventricular septal defect at 97.7% (95% CI 93.5–99.8). With the exception of tetralogy of Fallot ($I^2=0.0\%$, $P=0.957$) and single ventricle ($I^2=26.9\%$, $P=0.250$), there was significant heterogeneity of survival estimates among articles (Table 2). It was possible to calculate pooled 15-year survival estimates for aortic valve atresia or stenosis, atrioventricular septal defect, common arterial trunk, and coarctation of aorta but not for any other CHD subtypes. There were too few studies to calculate pooled survival beyond age 15 years, although in the few studies that reported survival into adulthood, survival was still gradually declining.

For subtypes for which just 3 studies reported survival, pooled estimates were also calculated using fixed-effect meta-analysis (Table 2). Pooled survival estimates were generally similar for the random- and fixed-effects models, with the exception of the 10- and 15-year pooled estimates for common arterial trunk (28.9% versus 35.4% and 36.5% versus 54.4%, respectively).

Quality Appraisal

Quality appraisal is shown in Table 3. All articles satisfied the study ascertainment domain because, by definition, population-based studies are representative of the population. The attrition domain was satisfied by 31% of articles because of studies failing to report the proportion of untraced cases; however, many of the studies classed unmatched cases as alive, so it is possible that all cases were traced. The outcome ascertainment domain was satisfied by 94% of studies, and the analysis domain was satisfied by 81%. Studies that did not satisfy the analysis domain were those that did not perform survival analysis and instead reported the proportion alive, which does not account for case censorship. This may have slightly inflated survival in these studies.

Table 2. Survival Estimates at Age One to 25

Subtype	Article	N	Survival Estimates (95% CI)						
			1 year	5 years	10 years	15 years	20 years	25 years	
All congenital heart disease	Dastgiri et al ²⁰	1069	78.4 (75.8–80.8)*	74.7 (73.8–75.5) [†]					
	Jackson et al ²⁵	1543	86.1 (84.3–87.8)*	82.0 (81.0–83.0)	80.4 (79.5–81.7) [†]				
	Meberg et al ²⁶	360	91.4 (88.0–94.1)*	88.9 (85.2–91.9)*					
	Moons et al ²⁸	921	96.0 (94.5–97.2)*	95.6 (94.0–96.8)*					
	Nembhard et al ²⁹	19 530		90.7 (90.2–91.1)*					
	Olsen et al ³⁰	6646	80 (79–81)	76 (75–77)*	75 (74–76)			72 (70–73)	
	Samanek et al ³¹	5030	80.0 (78.9–81.1)	77.8 (76.6–79.0)	77.4 (76.2–78.5)	77.1 (75.9–78.3)			
	Tennant et al ³²	4281	92.3 (91.5–93.1)	91.1 (90.2–91.9)	90.8 (89.9–91.6)	90.3 (89.3–91.2)	89.5 (88.4–90.6)		
	Pooled estimate (95% CI)		87.0 (82.1–91.2)	85.4 (79.4–90.5)	81.4 (73.8–87.9)				
	Heterogeneity I ² & P-value		99.0%, P<0.001	99.6%, P<0.001	99.5%, P<0.001				
Ventricular septal defect	Garne ²³	195		96.9 (93.4, 98.9)*					
	Moons et al ²⁸	303		99.3 (97.6–99.9)*					
	Nembhard et al ²⁹	10 382		93.9 (93.5–94.4)*					
	Olsen et al ³⁰	1559	94 (93–95)		90 (89–91.7)				
	Samanek et al ³¹	2092	91.1 (89.8–92.3)*			89.4 (88.0–90.7)			
	Tennant et al ³²	1805	99.2 (98.7–99.5)	99.1 (98.6–99.5)	99.1 (98.5–99.4)	99.1 (98.5–99.4)	98.3 (96.6–99.1)		
	Pooled estimate (95% CI)		95.5 (89.0–99.2)	97.7 (93.5–99.8)					
			95.5 (95.0–96.0)						
	Heterogeneity I ² & P-value		99.0%, P<0.001	98.1%, P<0.001					
	Pulmonary valve stenosis	Garne ²³	33		97.0 (84.2–99.9)*				
Nembhard et al ²⁹		1170		91.6 (89.9–93.1)*					
Samanek et al ³¹		292	96.2 (94.0–98.5)	95.6 (93.1–98.0)	95.6 (93.1–98.0)	95.6 (93.1–98.0)			
Tennant et al ³²		382	98.7 (96.8–99.5)	98.1 (96.1–99.1)	98.1 (96.1–99.1)	98.1 (96.1–99.1)	98.1 (96.1–99.1)		
Pooled estimate (95% CI)				95.6 (91.1–98.6)					
Heterogeneity I ² & P-value				89.6%, P<0.001					
Atrial septal defect	Garne ²³	78		98.7 (93.1, 100.0)*					
	Moons et al ²⁸	162		99.4 (96.6–100.0)*					
	Nembhard et al ²⁹	9164		89.9 (89.3–90.5)*					
	Olsen et al ³⁰	361	93 (90–95.3)		91 (88–95.6)			84 (72–91)	

Continued

Table 2. Continued

Subtype	Article	N	Survival Estimates (95% CI)					
			1 year	5 years	10 years	15 years	20 years	25 years
Aortic valve atresia/stenosis	Samanek et al ³¹	436	94.0 (92.4–96.3)		92.9 (90.1–95.1)*	92.9 (90.1–95.1)*		
	Tennant et al ³²	365	97.3 (95.0–98.5)	97.0 (94.6–98.3)	97.0 (94.6–98.3)	96.3 (93.3–98.0)	96.3 (93.3–98.0)	
	Pooled estimate (95% CI)		94.9 (92–97.2)	96.8 (90.8–99.7)	94.0 (89.9–97.1)			
			94.8 (93.5–96.0)	95.4%, <i>P</i> <0.001	94.3 (92.7–95.6)			
	Heterogeneity I ² & <i>P</i> -value		77.4%, <i>P</i> <0.001		81.6%, <i>P</i> =0.004			
	Garne ²³	24		87.5 (67.6, 97.3)*				
	Moons et al ²⁸	36		100.0 (90.3–100.0)*				
	Samanek ³¹	391	90.3 (87.3–93.3)			88.4 (85.1–91.7)		
	Tennant et al ³²	171	92.4 (87.3–95.5)	91.2 (85.9–94.6)	91.2 (85.9–94.6)	89.3 (83.2–93.3)	89.3 (83.2–93.3)	
	Wang et al ³³	877				74.1 (71.0–77.0)		73.4 (70.1–76.4)
Atrioventricular septal defect	Wang et al ³⁵	2646	83.6 (82.1–84.9)	81.5 (79.7–83.2)				
	Pooled estimate (95% CI)		88.7 (82.4–93.8)	92.1 (81.3–98.4)		84.4 (73.1–93.1)		
			85.0 (83.7–86.2)	92.7%, <i>P</i> <0.001		82.2 (80.3–84.0)		
	Heterogeneity I ² & <i>P</i> -value		91.3%, <i>P</i> <0.001			96.8%, <i>P</i> <0.001		
	Frid et al ²²	502	77.1 (73.2–80.7)*	66.5 (62.2–70.7)*	64.3 (59.9–68.5)*	63.1 (58.8–67.4)*		
	Garne ²³	20		50 (27.2–72.8)*				
	Miller et al ²⁷	338			57.9 (49.7–65.3)			
	Moons et al ²⁸	37		91.9 (78.1–98.3)*				
	Olsen et al ³⁰	354	75 (70–79)		65 (59–70)			59 (51–65)
	Samanek et al ³¹	201	62.2 (55.4–69.0)	54.7 (47.7–61.8)	54.2 (47.1–61.2)	54.2 (47.1–61.2)		
Coarctation of aorta	Tennant et al ³²	94	84.0 (74.9–90.1)	80.9 (71.3–87.5)	79.7 (70.1–86.6)	79.7 (70.1–86.6)	79.7 (70.1–86.6)	
	Wang et al ³³	1004				59.5 (56.3–62.6)	58.1 (56.5–61.4)	56.6 (52.8–60.2)
	Wang et al ³⁴	4884	80.1 (79.0–81.2)	76.7 (75.3–78.1)				
	Pooled estimate (95% CI)		75.9 (70.5–81.0)	71.2 (61.9–79.6)	64.0 (57.2–70.5)	63.4 (56.3–70.3)		
	Heterogeneity I ² & <i>P</i> -value		89.0%, <i>P</i> <0.001	92.7%, <i>P</i> <0.001	81.4%, <i>P</i> <0.001	85.9%, <i>P</i> <0.001		
	Garne ²³	12		58.3 (27.7–84.8)*				
	Moons et al ²⁸	46		91.3 (79.2–97.6)*				
	Nembhard et al ²⁹	1145		78.6 (76.1–80.9)				
	Olsen et al ³⁰	334	84 (79–87)		82 (77–85)			78 (61–82)
	Samanek et al ³¹	266	68.0 (62.3–73.8)	65.4 (59.6–71.3)	65.0 (59.2–70.9)	65.0 (59.2–70.8)		
	Tennant et al ³²	189	91.5 (86.6–94.7)	91.5 (86.6–94.7)	90.9 (85.8–94.3)	90.9 (85.8–94.3)	89.6 (83.7–93.5)	

Continued

Table 2. Continued

Subtype	Article	N	Survival Estimates (95% CI)					10 years	15 years	20 years	25 years
			1 year	5 years							
	Wang et al ³³	2529	79.4 (77.8–81.0)	77.0 (75.4–78.6)					76.0 (74.3–77.7)		75.2 (73.3–77.0)
	Wang et al ³⁴	6365	84.5 (83.6–85.4)	81.9 (80.7–83.0)							
	Pooled estimate (95% CI)		82.7 (75.4–89.0)	81.0 (70.7–89.4)				80.3 (65.0–92.0)	78.2 (65.9–88.4)		
								79.5 (76.6–82.2)	76.2 (74.6–77.7)		
	Heterogeneity I^2 & P -value		93.7%, $P<0.001$	93.0%, $P<0.001$				87.3%, $P<0.001$	95.6%, $P<0.001$		
Common arterial trunk	Moons et al ²⁸	7		85.7 (42.1–99.6)*							
	Olsen et al ³⁰	78	45 (34–55)	45 (34–55)				45 (34–55)	45 (34–55)	45 (34–55)	45 (34–55)
	Samanek et al ³¹	55	12.7 (3.7–21.7)	10.5 (4.1–22.2)*				7.3 (0–15.4)	7.3 (0–15.4)		
	Tennant et al ³²	36	36.1 (21.0–51.4)	36.1 (21.0–51.4)				36.1 (21.0–51.4)			
	Wang et al ³³	460							59.2 (54.4–63.6)		55.2 (49.5–60.5)
	Wang et al ³⁵	956	75.1 (72.7–77.7)								
	Pooled estimate (95% CI)		41.8 (14.1–72.6)	47.4 (21.8–73.8)				28.9 (16.3–43.3)	36.5 (14.6–62)		
Pulmonary valve atresia (with IVS)	Heterogeneity I^2 & P -value		97.6%, $P<0.001$	96.3%, $P<0.001$				87.3%, $P<0.001$	94.5%, $P<0.001$		
	Fixler et al ²¹	118	59.3 (49.9–67.6)	55.7 (45.8–64.4)							
	Idorn et al ²⁴	75	41.7 (30.1–53.3)*	37.5 (26.4–49.2)*				35.3 (24.0–46.5)*	37.5 (26.4–49.2)*	35.3 (24.0–46.5)*	37.5 (26.4–49.2)*
	Moons et al ²⁸	6		83.3 (36.5–99.1)*							
	Samanek et al ³¹	53	18.9 (8.1–29.6)	7.6 (0.3–14.8)				7.6 (0.3–14.8)	7.6 (0.3–14.8)		
	Pooled estimate (95% CI)		39.7 (18.5–63.3)	41.1 (17.2–67.6)							
			45.5 (39.2–52.0)								
Pulmonary atresia	Heterogeneity I^2 & P -value		92.1%, $P<0.001$	92.0%, $P<0.001$							
	Garne et al ²³	5		60.0 (14.7–94.7)*							
Pulmonary valve atresia (with VSD)	Moons et al ²⁸	6	67 (19–96)*	50 (11.8–88.2)*							
	Samanek et al ³¹	55	61.8 (48.7–74.9)	54.5 (41.1–68.0)				45.2 (30.8–59.6)	45.2 (30.8–59.6)		
	Garne ²³	7		82.6 (61.2–95.0)*							
Tetralogy of Fallot	Moons et al ²⁸	52	83 (70–92)*	82.7 (69.7–91.8)*							
	Olsen et al ³⁰	381	83 (79–87)					70 (65–74)			67 (58–74)
	Samanek et al ³¹	169	84.6 (79.0–90.2)					76.6 (70.1–83.2)	76.6 (70.1–83.2)		
	Tennant et al ³²	190	90.5 (85.4–93.9)	83.7 (77.6–88.2)				83.1 (76.9–87.7)	83.1 (76.9–87.7)	80.8 (72.8–86.6)	

Continued

Table 2. Continued

Subtype	Article	N	Survival Estimates (95% CI)					15 years	20 years	25 years
			1 year	5 years	10 years					
	Wang et al ³⁴	5208	87.1 (86.1–87.9)	84.7 (83.5–85.8)						
	Wang et al ³⁴	1739								86.9 (85.3–88.4)
	Pooled estimate (95% CI)		86.3 (83.7–88.6)	84.6 (83.5–85.7)	81.4 (77.5–85)					
					81.6 (78.6–84.4)					
	Heterogeneity I ² & P-value		0.0%, P=0.097	0.0%, P=0.957	36.1%, P=0.209					
Total anomalous pulmonary venous return	Garne ²³	5		20 (0.5–71.6)*						
	Samanek et al ³¹	40	52.5 (36.7–82.3)	50.0 (34.2–65.8)	50.0 (34.2–65.8)	50.0 (34.2–65.8)				
	Tennant et al ³²	54	72.2 (58.2–82.2)	72.2 (58.2–82.2)	72.2 (58.2–82.2)	72.2 (58.2–82.2)	72.2 (58.2–82.2)			
	Pooled estimate (95% CI)			53.7 (30–76.6)						
				61.2 (51.2–70.6)						
Heterogeneity I ² & P-value				76.6%, P=0.014						
	Garne ²³	21		76.2 (52.8, 91.8)*						
	Moons et al ²⁸	29		100.0 (88.1–100.0)*						
	Olsen et al ³⁰	461	74 (70–78)		62 (38–67)				50 (41–59)	
	Samanek et al ³¹	271	61.6 (56.7–67.5)	56.5 (50.3–62.4)*	53.9 (46.8–60.9)	53.9 (46.8–60.9)				
Transposition of the great vessels	Tennant et al ³²	189	82.5 (76.3–87.3)	81.0 (74.6–85.9)	80.3 (73.8–85.3)	78.4 (71.6–83.9)	74.1 (64.4–81.5)			
	Wang et al ³⁴	1840								74.5 (72.4–76.4)
	Wang et al ³⁴	4330	83.7 (82.6–84.4)	81.1 (79.7–82.4)						
	Pooled estimate (95% CI)		76.0 (65.5–85.1)	81.9 (68.9–91.9)	66.1 (46.0–83.5)					
						67.1 (62.5–71.5)				
Tricuspid atresia	Heterogeneity I ² & P-value		96.9%, P<0.001	95.9%, P<0.001	93.6%, P<0.001					
	Fixler et al ²¹	67	76.1 (64.0–84.6)	74.6 (62.4–83.4)						
	Idom et al ²⁴	106	68.0 (58.2–76.7)*	61.7 (51.4–70.6)*	60.5 (50.4–69.7)*	57.4 (47.6–67.1)*	57.4 (47.6–67.1)*			57.4 (47.6–67.1)*
	Moons et al ²⁸	4	100 (39.8–100.0)*	100 (39.8–100.0)*						
	Samanek et al ³¹	39	46.2 (30.2–62.1)		35.9 (20.5–51.3)	35.9 (20.5–51.3)				
	Tennant et al ³²	24	83.3 (61.5–93.4)	66.7 (44.3–81.7)	62.5 (40.3–78.4)	62.5 (40.3–78.4)				
	Pooled estimate (95% CI)		71.4 (57.2–83.7)	53.7 (30.0–76.6)	53.1 (36.5–69.2)	53.3 (37.2–69.1)				
					55.1 (47.3–62.9)	56.2 (49.1–63.1)				
	Heterogeneity I ² & P-value		74.4%, P=0.004	93.9%, P<0.001	72.4%, P=0.027	72.9%, P=0.025				
				4.5 (0.1–22.8)*						
Hypoplastic left heart	Garne	22								
	Idom et al ²⁴	252	12.5 (8.9–17.5)*	10.4 (6.9–14.8)*	10.4 (6.9–14.8)*	8.8 (5.6–12.9)*				

Continued

Table 2. Continued

Subtype	Article	N	Survival Estimates (95% CI)					
			1 year	5 years	10 years	15 years	20 years	25 years
Single ventricle	Moons et al ²⁸	10	50 (18.7–81.3)*	40.0 (12.2–73.8)*				
	Samanek et al ³¹	172	0 (0.0–2.1)*	0 (0.0–2.1)*	0 (0.0–2.1)*	0 (0.0–2.1)*		
	Tennant et al ³²	73	4.1 (1.1–10.5)	2.9 (0.5–8.9)				
	Wang et al ³⁴							33.1 (30.6–35.7)
	Wang et al ³⁴	2976	55.2 (53.4–56.9)	50.6 (48.4–52.7)				
	Pooled estimate (95% CI)		17.4 (0.0–54.5)	12.5 (0.0–41.4)				
	Heterogeneity I ² & P-value		99.5%, P<0.001	99.1%, P=0.036				
	Fixler et al ²¹	286	64.7 (58.8–69.9)	56.1 (49.9–61.7)				
	Garne ²³	16		56.3 (29.9–80.2)*				
	Moons et al ²⁸	9	56 (21–86)*	55.6 (21.2–86.3)*				
Ebstein's anomaly	Tennant et al ³²	31	83.9 (65.5–93.0)	74.2 (55.0–86.2)	74.2 (55.0–86.2)	64.5 (43.1–80.0)		
	Pooled estimate (95% CI)		70.4 (54.1–84.4)	59.8 (50.4–68.8)				
			69.5 (63.3–75.3)					
	Heterogeneity I ² & P-value		65.0%, P=0.057	26.9%, P=0.250				
	Garne ²³	5		60.0 (14.7–94.7)*				
	Moons et al ²⁸	3		100 (29.2–100.0)*				
	Nembhard et al ²⁹	160		68.8 (61.0–75.8)*				
	Samanek et al ³¹	22	67.9 (50.2–86.5)	64.3 (46.2–82.4)	64.3(46.2–82.4)	64.3(46.2–82.4)		
	Tennant et al ³²	55	67.3 (53.2–78.0)	58.0 (43.8–69.7)	58.0 (43.8–69.7)	54.6 (39.7–67.2)	54.6 (39.7–67.2)	
	Pooled estimate (95% CI)			65.6 (57.5–73.2)				
	Heterogeneity I ² & P-value			18.0%, P=0.300				

Pooled estimates are calculated using random effects meta-analysis. But where there are ≤3 studies, pooled estimates are also calculated using fixed effects meta-analysis with these results being shown in italics. AVA/S in Wang et al's studies refers to aortic valve stenosis only. IVS indicates intact ventricular septum; VSD, ventricular septal defect.

*Indicates that 95% CIs were not reported in the study, but 95% binomial exact 95% CIs were calculated by the authors.

[†]95% CIs obtained from author

Table 3. Quality Appraisal of Included Articles

Domain	Quality Items, Potential Bias	Yes	No	Not Stated	Number of Studies, %
Study ascertainment	The study population is adequately described for key characteristics (ie, CHD subtype frequency, sex distribution, ethnicity)	21–23,25,27,29,30,33,34	20,24,26–28,31,32,35		9 (56%)
	Ascertainment is adequately described, including method of ascertainment included birth years, study location	20–35			16 (100%)
	Inclusion and exclusion criteria are adequately described (ie, ICD codes stated and inclusion of extracardiac anomalies)	21–27,29,30,32–35	20,27,28,31		13 (81%)
	There is adequate ascertainment	20–35			16 (100%)
Study attrition	POTENTIAL BIAS: The study sample represents the population of interest on key characteristics sufficient to limit potential bias to the results	20–35			16 (100%)
	The proportion of traced cases is stated and adequate	20,22,23,29,32		21,24–28,30,31,33–35	5 (31%)
	Reasons for untraced cases are provided	20,23,29,32	22	21,24–28,30,31,33–35	4 (25%)
	Untraced cases are adequately described for key characteristics (ie, CHD subtype)	20,22,23,29,32		21,24–28,30,31,33–35	5 (31%)
	There are no important differences between key characteristics and outcomes in participants who were traced and untraced			20–35	0 (0%)
Outcome ascertainment	POTENTIAL BIAS: Untraced cases are not associated with key characteristics (ie, the study data adequately represent the sample), sufficient to limit potential bias	20,22,23,29,32		21,24–28,30,31,33–35	5 (31%)
	Frequency of outcome is recorded	20–29,32–35	30,31		14 (88%)
	The method of ascertainment of deaths is valid and reliable to limit misclassification bias	20–35		25	15 (94%)
	POTENTIAL BIAS: The outcome of interest is adequately measured in study participants to sufficiently limit potential bias	20–35		25	15 (94%)
Analysis	There is sufficient presentation of results (ie, number of cases and 95% CIs)	21,24,25,27,29–35	20,22,23,26–28		11 (69%)
	The analysis is adequate for the design of the study	20,21,24,25,27–35	22,23,26		13 (81%)
	Results are not selectively reported	20–35			16 (100%)
	POTENTIAL BIAS: The statistical analysis is appropriate for the design of the study, limiting potential for presentation of invalid results	20,21,24,25,27–35	22,23,26		13 (81%)

CHD indicates congenital heart disease; ICD, International Classification of Disease.

Discussion

In this systematic review and meta-analysis, we found that 87.0% of individuals born with CHD survived to age 1 year, 85.4% survived to age 5 years, and 81.4% survived to age 10 years. Few studies reported survival beyond age 10 years, but survival appeared to continue to gradually decrease into adulthood. There was substantial variation in survival estimates among articles, some of which was accounted for by study period, which positively affected survival.

The main strength of this systematic review is its restriction to population-based studies. Although including hospital-based studies would have increased the amount of data available, such studies underascertain milder CHD subtypes that do not require major medical intervention. In addition, children with severe CHD may travel to centers with specialist expertise; therefore, the survival estimates reported by hospital-based studies can be unrepresentative of the general population of individuals with CHD. The robustness of the individual rates of bias was examined using a quality assessment with previously published domains and items.¹⁹ Although each study failed to satisfy at least 1 quality item because of the population-based study designs, the potential for bias in each domain remained low. Moreover, for all CHD, we did not identify any significant publication bias according to the Egger test.

A further strength is the comprehensive nature of our search strategy. Three databases were searched for relevant citations, along with key journals and reference lists; therefore, the likelihood of missing key studies was limited. Full articles were reviewed by both authors to ensure that they fully met the inclusion criteria and that data were extracted correctly. A further strength is that we reported pooled estimates calculated from fixed- and random-effects meta-analyses if there were just 3 studies reporting survival. Random-effects meta-analysis may calculate pooled estimates using an imprecise between-study variance if the number of studies is low.¹⁵ The pooled estimates from the fixed-effect meta-analyses were broadly similar to those from the random-effects meta-analyses but with smaller confidence intervals.

There were also several limitations. The maximum follow-up was just 30 years, with 5 of the included studies reporting survival to just 5 years. The greatest risk of death occurred in infancy, but survival continued to decrease over follow-up, although at a much lesser rate. A study of CHD-related mortality rates between 1999 and 2006 in the United States showed a high mortality rate of 41.5 per 100 000 in infancy, which decreased to 1.38 between ages 1 and 4 years and stabilized at ≈ 0.55 between the ages of 5 and 65 years. After age 65 years, the mortality rate doubled to 1.10 per 100 000.³⁶

A further limitation is that longer term survival estimates may not be representative of children born with CHD today.

Even in the most recent studies, 25-year survival rates related to persons born in the 1990s; in our metaregression of 1-, 5-, and 10-year survival, we showed that survival estimates improved over time.

All included studies were performed in high-income Western populations. Evidence suggests that infant mortality rates associated with congenital anomalies are greater in low-income countries.³⁷ Consequently, the survival estimates in this review are not likely to be globally representative. Although we included only articles written in the English language, we did not identify any relevant articles written in other languages.

Most of the included articles included cases with extracardiac anomalies^{20–31,33,34}; therefore, it is difficult to assess how much of the mortality was accounted for by CHD as opposed to the co-occurring congenital anomalies. Nevertheless, cases with extracardiac anomalies accounted for only 20% of cases, and some extracardiac anomalies were not likely to be life threatening; therefore, the impact on survival is likely to be low. All articles used all-cause mortality, meaning that deaths may not have been directly related to the CHD diagnosis.

Although this review provides insight into long-term mortality associated with CHD, we did not account for morbidity. Research suggests that quality of life is lower in those with CHD and that those who live with CHD can have morbidities such as endocarditis, cerebrovascular accidents, myocardial infarctions, and arrhythmias.^{38–40} The American Heart Association has also reported that children with CHD are at increased risk of developmental disorders.⁴¹ Research suggests that children with CHD are more likely to require special education services, regardless of CHD severity.⁴²

In our metaregression, we found that a more recent study period positively affected survival estimates; however, even after adjustment for study period, there was still a high degree of heterogeneity. Although we adjusted for study period using the year of study commencement, the lengths of the study periods varied by article; therefore, our adjustment for the year of study commencement is not likely to have fully accounted for the changes in survival over time. Further heterogeneity is likely attributable to a variety of sources. Case ascertainment is likely a major cause. Olsen et al reported lower survival estimates even after accounting for study period, but their prevalence of CHD was almost half that of other studies. Given that they included only cases diagnosed before age 1 year, it is likely that they underascertained cases with milder CHD subtypes, such as ventricular septal defect.³⁰ The data sources used may also have contributed to variation in ascertainment, with articles using hospital records as opposed to congenital anomaly registers (which use multiple sources for ascertainment) contributing to lower survival estimates, likely due to the milder cases being underascertained.³¹

Variation in study periods is arguably the greatest source of heterogeneity for survival estimates. Survival has improved over time because of advances in surgical correction. The Fontan operation, for example, for repair of single ventricle, hypoplastic left heart, and tricuspid atresia and the conduit repair for cases of common arterial trunk were introduced in the late 1970s and developed throughout the 1980s and 1990s.^{43,44} The arterial switch operation for treatment of transposition of the great vessels was introduced in 1975⁴⁵ and fully replaced the atrial switch operations in the early 1990s, resulting in improved long-term survival.⁴⁶ Survival is also likely to have improved over time because of advances in prenatal diagnosis. Greater prenatal diagnosis rates may have led to an increase in rates of termination (for fetal anomaly). If cases with the more severe subtypes were terminated, this would have resulted in better survival. Prenatal diagnosis also allows quicker intervention at birth or even in utero, which may also improve survival.⁴⁷ In addition, survival is likely to have improved because of the introduction of prostaglandin, which underwent trials in neonates with cyanotic CHD in the 1970s,^{48,49} although it was not frequently administered until the 1980s.

The improvement in survival rates over time has led to an emerging population of adolescents and adults with CHD. These patients require long-term follow-up, sometimes leading to reinvestigation and reoperation. Consequently, population-based surveillance of CHD is crucial to adequately assess the variety of health and social services required by those with CHD throughout their lives.

Acknowledgments

Thanks to Harper Gilmour, Saeed Dastgiri, Wendy Nembhard, Philip Moons and Ying Wang for providing further information on their studies. We thank Dr Svetlana Glinianaia, Prof Fiona Matthews and Dr Angela McBrien for their helpful comments on this manuscript.

Sources of Funding

Best is funded by the British Heart Foundation (FS/12/23/29511).

Disclosures

None.

References

- Hoffman JIE, Kaplan S. The incidence of congenital heart disease. *J Am Coll Cardiol*. 2002;39:1890–1900.
- Reller MD, Strickland MJ, Riehle-Colarusso T, Mahle WT, Correa A. Prevalence of congenital heart defects in metropolitan Atlanta, 1998–2005. *J Pediatr*. 2008;153:807–813.
- Dolk H, Loane M, Garne E. Congenital heart defects in Europe: prevalence and perinatal mortality, 2000 to 2005. *Circulation*. 2011;123:841–849.
- Centers for Disease Control Prevention. Racial differences by gestational age in neonatal deaths attributable to congenital heart defects—United States, 2003–2006. *MMWR Morb Mortal Wkly Rep*. 2010;59:1208.
- Oster ME, Lee KA, Honein MA, Riehle-Colarusso T, Shin M, Correa A. Temporal trends in survival among infants with critical congenital heart defects. *Pediatrics*. 2013;131:e1502–e1508.
- Bourdial H, Jamal-Bey K, Edmar A, Caillet D, Wuillai F, Bernede-Bauduin C, Boumahni B, Robillard PY, Kauffmann E, Laffitte A, Touret Y, Cuillier F, Fourmaintraux A, Alessandri JL, Gérardin P, Randrianaivo H. Congenital heart defects in La Réunion Island: a 6-year survey within a EUROCAT-affiliated congenital anomalies registry. *Cardiol Young*. 2012;22:547–557.
- Dadvand P, Rankin J, Shirley MDF, Rushton S, Pless-Mullooli T. Descriptive epidemiology of congenital heart disease in Northern England. *Paediatr Perinat Epidemiol*. 2009;23:58–65.
- Dilber D, Malcic I. Spectrum of congenital heart defects in Croatia. *Eur J Pediatr*. 2010;169:543–550.
- Cleves MA, Ghaffar S, Zhao W, Mosley BS, Hobbs CA. First-year survival of infants born with congenital heart defects in Arkansas (1993–1998): a survival analysis using registry data. *Birth Defects Res A Clin Mol Teratol*. 2003;67:662–668.
- Lee K, Khoshnood B, Chen L, Wall SN, Cromie WJ, Mittendorf RL. Infant mortality from congenital malformations in the United States, 1970–1997. *Obstet Gynecol*. 2001;98:620–627.
- Knowles RL, Bull C, Wren C, Wade A, Goldstein H, Dezateux C. Modelling survival and mortality risk to 15 years of age for a national cohort of children with serious congenital heart defects diagnosed in infancy. *PLoS One*. 2014;9:e106806.
- Verheugt CL, Uiterwaal CSPM, Grobbee DE, Mulder BJM. Long-term prognosis of congenital heart defects: a systematic review. *Int J Cardiol*. 2008;131:25–32.
- Parmar MK, Torri V, Stewart L. Extracting summary statistics to perform meta-analyses of the published literature for survival endpoints. *Stat Med*. 1998;17:2815–2834.
- Plot Digitizer. 2015. Available at: <http://plotdigitizer.sourceforge.net/>. Accessed June 2015.
- Borenstein M, Hedges L, Rothstein H. Introduction to meta-analysis. 2007.
- Barendregt JJ, Doi SA, Lee YY, Norman RE, Vos T. Meta-analysis of prevalence. *J Epidemiol Community Health*. 2013;67:974–978.
- Higgins J, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ*. 2003;327:557–560.
- Egger M, Smith GD, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ*. 1997;315:629–634.
- Hayden JA, Côté P, Bombardier C. Evaluation of the quality of prognosis studies in systematic reviews. *Ann Intern Med*. 2006;144:427–437.
- Dastgiri S, Gilmour WH, Stone DH. Survival of children born with congenital anomalies. *Arch Dis Child*. 2003;88:391–394.
- Fixler DE, Nembhard WN, Salemi JL, Ethen MK, Canfield MA. Mortality in first 5 years in infants with functional single ventricle born in Texas, 1996 to 2003. *Circulation*. 2010;121:644–650.
- Frid C, Bjorkhem G, Jonzon A, Sunnegardh J, Anneren G, Lundell B. Long-term survival in children with atrioventricular septal defect and common atrioventricular valvar orifice in Sweden. *Cardiol Young*. 2004;14:24–31.
- Garne E. Congenital heart defects—occurrence, surgery and prognosis in a Danish County. *Scand Cardiovasc J*. 2004;38:357–362.
- Idorn L, Olsen M, Jensen AS, Juul K, Reimers JJ, Sorensen K, Johnsen SP, Sondergaard L. Univentricular hearts in Denmark 1977 to 2009: incidence and survival. *Int J Cardiol*. 2013;167:1311–1316.
- Jackson M, Walsh KP, Peart I, Arnold R. Epidemiology of congenital heart disease in Merseyside—1979 to 1988. *Cardiol Young*. 1996;6:272–280.
- Meberg A, Otterstad JE, Froland G, Lindberg H, Sorland SJ. Outcome of congenital heart defects—a population-based study. *Acta Paediatr*. 2000;89:1344–1351.
- Miller A, Siffel C, Lu C, Riehle-Colarusso T, Frías JL, Correa A. Long-term survival of infants with atrioventricular septal defects. *J Pediatr*. 2010;156:994–1000.
- Moons P, Sluysmans T, De Wolf D, Massin M, Suys B, Benatar A, Gewillig M. Congenital heart disease in 111 225 births in Belgium: birth prevalence, treatment and survival in the 21st century. *Acta Paediatr*. 2009;98:472–477.
- Nembhard WN, Salemi JL, Ethen MK, Fixler DE, Dimaggio A, Canfield MA. Racial/Ethnic disparities in risk of early childhood mortality among

- children with congenital heart defects. *Pediatrics*. 2011;127:e1128–e1138.
30. Olsen M, Christensen TD, Pedersen L, Johnsen SP, Hjortdal VE. Late mortality among Danish patients with congenital heart defect. *Am J Cardiol*. 2010;106:1322–1326.
 31. Samanek M, Voriskova M. Congenital heart disease among 815,569 children born between 1980 and 1990 and their 15-year survival: a prospective Bohemia survival study. *Pediatr Cardiol*. 1999;20:411–417.
 32. Tennant PW, Pearce MS, Bythell M, Rankin J. 20-year survival of children born with congenital anomalies: a population-based study. *Lancet*. 2010;375:649–656.
 33. Wang Y, Hu J, Druschel CM, Kirby RS. Twenty-five-year survival of children with birth defects in New York State: a population-based study. *Birth Defects Res Part A Clin Mol Teratol*. 2011;91:995–1003.
 34. Wang Y, Liu G, Druschel CM, Kirby RS. Maternal race/ethnicity and survival experience of children with congenital heart disease. *J Pediatr*. 2013;163:1437–1442.e1431–1432.
 35. Wang Y, Liu G, Canfield MA, Mai CT, Gilboa SM, Meyer RE, Anderka M, Copeland GE, Kucik JE, Nembhard WN, Kirby RS. Racial/ethnic differences in survival of United States children with birth defects: a population-based study. *J Pediatr*. 2015;166:819–826.e812.
 36. Gilboa SM, Salemi JL, Nembhard WN, Fixler DE, Correa A. Mortality resulting from congenital heart disease among children and adults in the United States, 1999 to 2006. Clinical perspective. *Circulation*. 2010;122:2254–2263.
 37. Rosano A, Botto LD, Botting B, Mastroiacovo P. Infant mortality and congenital anomalies from 1950 to 1994: an international perspective. *J Epidemiol Community Health*. 2000;54:660–666.
 38. Knowles RL, Day T, Wade A, Bull C, Wren C, Dezateux C; Defects UKCSOCH. Patient-reported quality of life outcomes for children with serious congenital heart defects. *Arch Dis Child*. 2014;99:413–419.
 39. Engelfriet P, Boersma E, Oechslin E, Tijssen J, Gatzoulis MA, Thilén U, Kaemmerer H, Moons P, Meijboom F, Popelová J. The spectrum of adult congenital heart disease in Europe: morbidity and mortality in a 5 year follow-up period the Euro Heart Survey on adult congenital heart disease. *Eur Heart J*. 2005;26:2325–2333.
 40. Warnes CA. The adult with congenital heart disease: born to be bad? *J Am Coll Cardiol*. 2005;46:1–8.
 41. Marino BS, Lipkin PH, Newburger JW, Peacock G, Gerdes M, Gaynor JW, Mussatto KA, Uzark K, Goldberg CS, Johnson WH. Neurodevelopmental outcomes in children with congenital heart disease: evaluation and management: a scientific statement from the American Heart Association. *Circulation*. 2012;126:1143–1172.
 42. Riehle-Colarusso T, Autry A, Razzaghi H, Boyle CA, Mahle WT, Braun KVN, Correa A. Congenital heart defects and receipt of special education services. *Pediatrics*. 2015;136:496–504.
 43. Girinath MR. Case presentation: truncus arteriosus: repair with homograft reconstruction in infancy. In: Barratt-Boyes BG, Neutze JM, Harris EA, eds. *Heart Disease in Infancy: Diagnosis and Surgical Treatment*. Edinburgh: Churchill Livingstone; 1973:234.
 44. Sanders JH Jr. Gibbon's surgery of the chest. *Arch Surg*. 1976;111:1411.
 45. Jatene AD, Fontes VF, Paulista PP, de Souza LC, Neger F, Galantier M, Souza JE. Successful anatomic correction of transposition of the great vessels. A preliminary report. *Arq Bras Cardiol*. 1975;28:461–464.
 46. Hörer J, Schreiber C, Cleuziou J, Vogt M, Prodan Z, Busch R, Holper K, Lange R. Improvement in long-term survival after hospital discharge but not in freedom from reoperation after the change from atrial to arterial switch for transposition of the great arteries. *J Thorac Cardiovasc Surg*. 2009;137:347–354.
 47. Freud LR, McElhinney DB, Marshall AC, Marx GR, Friedman KG, Pedro J, Emani SM, Lafranchi T, Silva V, Wilkins-Haug LE. Fetal aortic valvuloplasty for evolving hypoplastic left heart syndrome: postnatal outcomes of the first 100 patients. *Circulation*. 2014;130:638–645.
 48. Elliott RB, Starling MB, Neutze JM. Medical manipulation of the ductus arteriosus. *Lancet*. 1975;305:140–142.
 49. Olley PM, Coceani F, Bodach E. E-type prostaglandins: a new emergency therapy for certain cyanotic congenital heart malformations. *Circulation*. 1976;53:728–731.

Long-Term Survival of Individuals Born With Congenital Heart Disease: A Systematic Review and Meta –Analysis

Katie E. Best and Judith Rankin

J Am Heart Assoc. 2016;5:e002846; originally published June 16, 2016;
doi: 10.1161/JAHA.115.002846

The *Journal of the American Heart Association* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Online ISSN: 2047-9980

The online version of this article, along with updated information and services, is located on the World Wide Web at:

<http://jaha.ahajournals.org/content/5/6/e002846>

Subscriptions, Permissions, and Reprints: The *Journal of the American Heart Association* is an online only Open Access publication. Visit the Journal at <http://jaha.ahajournals.org> for more information.